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ARNOLD & PORTER LLP
ATTN: IP DOCKETING DEPT.
555 TWELFTH STREET, N.W.
WASHINGTON, DC 20004-1206

EXAMINER

MYERS, CARLA J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/819,091

Applicant(s)

CAO ET AL.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 8-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 4/25/06.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on April 25, 2006 has been entered.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 8-11 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific or well-established utility.

The claims are drawn to substantially purified nucleic acid molecules having the sequence of SEQ ID NO: 1 and to substantially purified nucleic acid molecules comprising a nucleic acid sequence having 90% to 100% identity to SEQ ID NO: 1. In view of the "% identity" language, the claims further encompass mutants, allelic and splice variants of SEQ ID NO: 1 and homologues of SEQ ID NO: 1 from non-Arabidopsis species (see pages 31-32 of the specification). The claimed nucleic acids

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are not supported by either a specific and substantial asserted utility or a well-established utility.

The specification discloses nucleic acids consisting of SEQ ID NOs. 1-51,470. Each of these nucleic acids was isolated from a library prepared from *Arabidopsis thaliana* tissue. The present claims are limited to nucleic acids comprising SEQ ID NO: 1 and nucleic acids having 90-100% identity with SEQ ID NO: 1. The specification does not state whether nucleic acid molecule of SEQ ID NO: 1 constitutes a complete open reading frame, does not identify the location of the start and stop codons.

The specification also does not set forth a particular biological activity of a putative protein encoded by SEQ ID NO: 1. In Table 1 (page 92), it is stated that the nucleic acid of SEQ ID NO: 1 shares 84% identity with an “unknown protein with Src homology 3 (SH3) domain profile.” There is no showing that the protein encoded by SEQ ID NO: 1 itself has a SH3 domain profile. Further, the recitation that the protein encoded by SEQ ID NO: 1 shares identity with a protein having a SH3 domain profile is not equivalent to a clear statement that the protein encoded by SEQ ID NO :1 has the same biological activity of the uncharacterized protein having a SH3 domain profile. Even if it is determined that the protein encoded by SEQ ID NO: 1 has a SH3 domain profile, the specification has not established that the presence of the SH3 domain profile imparts a specific biological activity to the encoded protein.

No specific biological activity has been disclosed for the “unknown protein” to which the presently encoded protein shares sequence identity. Even if a specific biological activity was provided for this protein, the classification of a protein based on

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amino acid sequence homology does not establish a specific and substantial use for the nucleic acids encoding that protein. Sequence and structural homology between different nucleotide and amino acid sequences are not necessarily correlated with functional activity since proteins having SH3 domains may have very distinct biological activities. See Whisstock et al, set forth below.

Additionally, the specification (page 39) states that the claimed nucleic acids can be used to obtain other nucleic acids from the same species or to isolate homologous nucleic acids from other species. However, such uses lack a specific and substantial utility. Such uses allow only for the identification and analysis of other nucleic acids. Because a utility has not been established for the present nucleic acid, the use of this nucleic acid to search for additional nucleic acids does not constitute a "real world" context of use.

The specification (page 39-40) further contemplates that the nucleic acid of SEQ ID NO: 1 can be used for mapping studies, linkage analysis, constructing transgenic plants, screening for traits or screening for polymorphisms. However, these uses are applicable to a broad class of molecules since all plant nucleic acids could be used for these purposes. Thereby, these uses are general and do not constitute a specific utility. While the use of the nucleic acid of SEQ ID NO: 1 in the disclosed methods may eventually lead one to the identification of useful traits or specific polymorphisms or may eventually allow for the generation of transgenic plants, such uses constitute further research and experimentation and do not provide a readily-available, specific and substantial real-world use.

It is also asserted that the nucleic acid of SEQ ID NO: 1 can be used for antisense methods to “prevent or reduce gene function” (see page 79 of the specification). However, since it is unclear as to the activity of the nucleic acid of SEQ ID NO: 1 and the protein encoded by SEQ ID NO: 1, the use of the claimed nucleic acids to block or prevent an unknown function constitutes further research. Thereby, the use of the claimed nucleic acids for antisense methods does not provide a substantial, real world use for the claimed nucleic acids.

It is contemplated that the nucleic acid of SEQ ID NO: 1 can be used to synthesize protein, which could then be used in conducting further research to characterize the protein. However, the need for such research clearly indicates that the protein is not provided in a form that can be currently utilized for a real world purpose. Identifying and studying the properties of a protein or the mechanisms in which the protein is involved does not constitute a specific and substantial utility.

The specification also suggests that the proteins encoded by the claimed nucleic acids could be used to generate antibodies which could be used for detection purposes. Again, because a utility has not been established for the nucleic acid or the protein encoded thereby, use of the protein to generate antibodies to isolate and study proteins constitutes a research project and does not provide a specific and substantial utility.

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement as it applies to nucleic acids. See In re Fisher 421 F.3d 1356, 76 USPQ2d 1225 (Fed. Cir. 2005). The Court held that 35 USC 101 requires a showing that a nucleic acid is both substantial and specific, stating that “not every ‘use’ that can be

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asserted will be sufficient to satisfy §101. “ The court emphasized that disclosing a substantial utility means “show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some further date after further research. Simply put, to satisfy the ‘substantial’ utility requirement, an asserted use must show that claimed invention has a significant and presently available benefit to the public.” Id. 76 USPQ2d at 1230.

The Fisher Court also held that none of the uses asserted by Applicants in that case were either substantial or specific because each of the “asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world.” The Court concluded that “granting a patent to Fisher for its five claimed ESTs would amount to a hunting license because the claimed ESTs can be used only to gain further information about the underlying genes and the proteins encoded for by those genes. The claimed ESTs themselves are not an end of Fisher’s research effort, but only tools to be used along the way in the search for a practical utility.”

The instant situation is analogous to that which was addressed in Fisher. In the present case, Applicants have not established that the claimed nucleic acid encodes for a protein with a specific and substantial biological activity, or that the nucleic acid or protein could be used to identify a particular trait or to detect a particular polymorphism or promoter of known function. Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. Applicant is

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directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Response to Arguments

In the response, Applicants traverse this rejection by arguing that the proteins encoded by SEQ ID NO: 1 have significant homology with a protein having a Src homology 3 (SH3) domain. It is argued that the skilled artisan would recognize that proteins with SH3 domains have a role in, for example, signal transduction. Applicants cite Sparks et al as providing evidence of the utility of proteins having a SH3 domain profile.

This argument has been fully considered but is not persuasive. First, it is noted that the specification provides a table, Table 1, in which it is disclosed that SEQ ID NO: 1 shares 84% identity with an "unknown protein with Src homology 3 (SH3) domain profile." There is no clear statement in the specification that SEQ ID NO: 1 is considered to encode for a protein having the same functional activity as that of the "unknown protein." The specification has also not established that proteins encoded by SEQ ID NO: 1 themselves have a SH3 domain profile. There is also no disclosure in the specification as originally filed that the proteins encoded by SEQ ID NO: 1 have signal transduction activity. The teaching that the protein encoded by SEQ ID NO: 1 shares identity with a protein having a SH3 domain profile is not equivalent to a clear and specific disclosure in the specification that such a protein has signal transduction activity.

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Even if it is determined that the protein encoded by SEQ ID NO: 1 has a SH3 domain profile, the specification has not established that the presence of a SH3 domain profile imparts a specific and substantial biological activity onto the protein. As discussed by Sparks, "Src homology 3 (SH3) domains are conserved protein modules 50-70 amino acids long found in a variety of proteins with important roles in signal transduction" (see abstract). The reference teaches that the SH3 domain mediates protein-protein interactions by binding specific ligand sequences in a target protein. Sparks emphasizes the fact that each SH3 domain has a unique ligand preference. Sparks also discloses a variety of different proteins having SH3 domains, including Src, Yes, Abl, cortactin, p53Bp2, PLC γ , Crk, and Grb2. Each of these proteins binds to a distinct ligand and has a very distinct biological activity (see page 1540 and 1542). In particular, the reference states that "we have determined that each SH3 domain prefers peptide ligands with distinct sequence characteristics. Specifically, we have found that the Src SH3 domain selects peptides sharing the consensus motif LXXRPLPX Ψ P, whereas YES SH3 selects Ψ XXRPLPXLP, Abl SH3 selects PPX Θ XPPP Ψ P, Cortactin SH3 selects +PP Ψ PXXPXWL, p53bp2 SH3 selects RPX Ψ P Ψ R+SXP, PLC γ SH3 selects PPVPPRPXXTL, Crk N-terminal SH3 selects Ψ P Ψ LP Ψ K and Grb2 N-terminal SH3 selects + Θ DPLPXLP. Accordingly, the teachings of Sparks support the finding that the presence of a SH3 domain in a protein does not impart a specific biological activity onto that protein. Rather, proteins having SH3 domains have very distinct ligand binding activities and very distinct biological activities. Thereby, the disclosure that proteins encoded by SEQ ID NO: 1 share sequence identity with an unknown protein having a

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SH3 domain profile does not apprise one of skill in the art of a specific and substantial biological activity associated with proteins encoded by SEQ ID NO: 1.

The response further argues that the nucleic acids can be used to identify markers and isolate promoters associated with proteins encoded by SEQ ID NO: 1. This argument has been fully considered but is not persuasive because such a use is not considered to be specific or substantial. The utility is not specific because it is a property of all plant nucleic acids that they could be used to search for and try to identify a polymorphism or promoter. Further, the asserted utility is not substantial because it is a utility that is performed only to accomplish additional research. As stated in Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), an invention does not have utility sufficient to satisfy §101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. Id at 534-35, 148 USPQ at 695. In the instant application, Applicants have not set forth a single promoter or marker which has been identified using the claimed EST of SEQ ID NO: 1. All discussions regarding polymorphisms/markers in the specification are generic in nature. There is no showing of a reasonable expectation that the claimed nucleic acids could in fact be used to identify a specific promoter or marker. Even if a marker could be identified using the claimed EST, the specification has not disclosed a specific and substantial use for such an uncharacterized marker. The specification does not disclose an association between any particular polymorphisms and any phenotypic trait. Polymorphisms are naturally occurring variations within sequences, which themselves may not have any meaningful use. To determine whether a nucleic acid contains a polymorphism would first require

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comparing the sequence of SEQ ID NO: 1 to other newly isolated nucleic acids. Then, upon identifying a nucleic acid variation, one would need to determine whether such a variation had any meaningful use – e.g., whether the variation was associated with a particular trait or characteristic of a particular strain of plant. Therefore, the nucleic acids of SEQ ID NO: 1 may only be used to search for polymorphisms and if such polymorphisms are identified then the functional/biological activities of the polymorphisms could potentially be elucidated. Such research projects do not constitute a “real-world” use in currently available form.

Applicants assert that the specification teaches that the nucleic acids may also be used as markers and probes; to identify and obtain nucleic acid homologues, in microarrays as gene-specific targets; for transformation of plants; to determine the level or expression of a protein or mRNA; to overexpress or suppress a desired protein. However, these utilities are all generic and are characteristic of all nucleic acids. Such uses do not constitute a specific utility. As with the use of a nucleic acid to detect polymorphisms, a substantial utility for the nucleic acid can only be elucidated once the function of the nucleic acid or the product encoded by the nucleic acid is determined. The present specification does not teach a specific functional or biological activity associated with the nucleic acid of SEQ ID NO: 1 or a protein encoded by SEQ ID NO: 1 or an association between the claimed nucleic acids and any particular condition in plants. In the absence of such information, the skilled artisan would not know how to interpret the results of methods which determine the expression of a mRNA or protein and would not know how to use a plant that was transformed with the claimed nucleic

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acids. Additionally, the use of the claimed nucleic acids as a probe to detect itself does not constitute a specific utility because the result of such a use would be meaningless without additional information regarding the significance of the nucleic acid. The use of the claimed nucleic acids to detect homologues in other plants and organisms such as alfalfa and barley, as argued at page 8 of the brief, is also not a substantial and specific utility. Since the functional activity of the presently claimed nucleic acids is unknown, and the functional activity of any putative homologues is unknown, the detection of such homologues does not provide an immediate benefit and serves only as a starting point for further research. In addition, the use of a nucleic acid in a microarray does not confer a patentable utility since all nucleic acids may be used in microarrays. Each of these asserted utilities are generic, rather than specific. Use of the claimed nucleic acids in the above manners would not be meaningful in the absence of information regarding the specific biological activity or significance of these nucleic acids.

As set forth above, the rejection is based on the finding that Applicants have not disclosed a substantial and specific or well-established utility for the claimed invention. The facts supporting this conclusion are clearly set forth throughout the rejection. The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 USPQ 689 (1966) wherein the court held that 35 U.S.C. 101 requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that :

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...[u]nless and until a process is refined and developed to this point where specific benefit exists in currently available form

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there is insufficient justification for permitting an Applicant to engross what may prove to be a broad field...a patent is not a hunting license...[I]t is not a reward for the search, but compensation for its successful conclusion."

In the present situation, Applicants have not arrived at a "successful conclusion" as to the actual functional role or significance of the claimed nucleic acids. Without such information, the claimed nucleic acids can only be used as a starting point for conducting further experiments to arrive at a "successful conclusion."

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-11 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Further, the claimed invention is not enabled because the function of the nucleic acid of SEQ ID NO: 1 cannot be reliably predicted on the basis that this nucleic acid shares sequence identity with a nucleic acid having SH3 domains, but having no known biological function. As discussed above, the presence of a SH3 domain does not impart a specific and substantial biological activity onto a protein because proteins having SH3 domains are significantly diverse with respect to the ligands that they bind and their overall functional activities.

Additionally, the function of a nucleic acid cannot be reliably predicted on the basis of its amino acid sequence alone. As discussed by Whisstock et al. (see abstract):

"...prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and/or structure between a protein of unknown function and one or more well-understood proteins. Alternative methods include inferring conservative patterns in members of a functionally uncharacterized family for which many sequences are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof."

Whisstock (page 311-312) further teaches that while information regarding a protein's sequence, structure, genomics and interaction patterns may be useful in guiding experimental investigations into protein function,

"...inferring protein function from knowledge of the function of a close homologue is like solving the clue of an American crossword puzzle. Finding the word that satisfies the definition may be difficult but the task in principle is straightforward. Working out the function of a protein from its sequence and structure is like solving the clue of a British crossword puzzle. It is by no means obvious which features of the definition are providing the real clues, as opposed to misleading ones. Also, for both types of puzzle and for the suggestion of a protein function, even if your answer appears to fit it may be wrong."

Regarding claims 8-11, the specification has not adequately taught one of skill in the art how to use nucleic acids which comprise a nucleic acid sequence which has 90% to less than 100% identity with SEQ ID NO: 1. Claims 8-11 encompass nucleic acids comprising a nucleic acid sequence having 90%-99.9% identity with a nucleic acid sequence of SEQ ID NO: 1. Since the claims allow for this level of sequence variation, the claims include nucleic acids from other species, naturally-occurring and non-naturally occurring mutated nucleic acids, allelic variants, and splice variants. The specification has not adequately taught one of skill in the art how to use this genus of

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nucleic acids. It is unpredictable as to what would be the functional activity of nucleic acids having 90% to 99.9% identity with SEQ ID NO: 1. It is well known that for nucleic acids as well as proteins that even a single nucleotide or amino acid change can destroy the function of the molecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable. In the absence of extensive information regarding the relationship between the structure and function of the molecule, one cannot determine a priori which sequence changes will effect functional activity and which will not. Therefore, the recitation of sequence similarity results is an unpredictable and thereby unreliable correspondence between the claimed nucleic acid and the reference nucleic acid. The specification has not established that species within this genus of nucleic acids have any particular biological activity and the specification has not provided sufficient guidance as to how to use the genus of claimed nucleic acids without undue experimentation.

Response to arguments:

The response argues that this rejection has been overcome by the arguments stated above regarding utility. However, for the reasons set forth above, it is maintained that the uses asserted for the claimed invention are an object of study and are not specific, nor substantial. The specification cannot enable or teach one how to use the invention within 35 U.S.C. 112, first paragraph, if there is no patentable utility within 35 U.S.C. 101. Because there is no utility for the claimed invention for the reasons set forth above, it is maintained that the specification has not enabled the claimed invention.

Further, regarding claims 8-11, the rejection has not been overcome because Applicant's have not adequately taught one of skill in the art how to make and use a representative number of the variant nucleic acids encompassed by the claims. No specific nucleic acids having 90%-99% identity with SEQ ID NO: 1 have been exemplified in the specification, and no specific biological activity has been established for such nucleic acids. Given the unpredictability of determining the effect of a nucleotide change on the function of a protein encoded thereby, it is highly unpredictable as to what would be the activity of a nucleic acid having 90-99% activity with SEQ ID NO: 1. Given this unpredictability and the lack of specific guidance provided by the specification, undue experimentation would be required to make and use nucleic acids having 90-99% identity with SEQ ID NO: 1.

4. Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to substantially purified nucleic acids comprising a sequence having between 90% to 100% identity to a nucleic acid sequence of SEQ ID NO: 1. The claims thereby encompass variants of SEQ ID NO: 1, including mutants, allelic and splice variants of SEQ ID NO: 1 and homologues of SEQ ID NO: 1 from non-Arabidopsis species (see pages 31-32 of the specification). While nucleic acids consisting of SEQ ID NO: 1 meet the written description requirements, the specification

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does not provide an adequate written description of the claimed genus of nucleic acids that share more than 90%, but less than 100% identity with SEQ ID NO: 1.

The specification (Table 1, page 92) teaches the nucleic acid sequence of SEQ ID NO: 1 and discloses that this nucleic acid shares 84% identity with an "unknown protein with Src homology 3 (SH3) domain profile." However, the specification has not established that the sequence of SEQ ID NO: 1 itself has a SH3 domain profile. Further, it has not been established that the presence of the SH3 domain profile imparts a specific biological activity to the encoded protein. No additional information is provided regarding the structural and functional properties of SEQ ID NO: 1. In particular, the specification does not state whether this nucleic acid molecule constitutes a complete open reading frame, does not identify the location of the start and stop codons and does not set forth a particular biological activity of a putative protein encoded by SEQ ID NO: 1. The specification does not disclose any specific variants or homologues of SEQ ID NO: 1 and does not exemplify any specific nucleic acids which have 90-99% identity with SEQ ID NO: 1.

The claims define the nucleic acids in terms of their structure, but do not define the nucleic acids in terms of their functional properties. Accordingly, the claims are inclusive of nucleic acid molecules which have distinct biological activities from the nucleic acid of SEQ ID NO: 1. The specification has not clearly set forth a biological activity for the nucleic acids of SEQ ID NO: 1. Further, the specification does not set for a biological activity for putative mutant and allelic variants or splice variants or homologues of SEQ ID NO: 1.

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The general knowledge in the art concerning homologues, mutants, allelic and splice variants does not provide any indication of how modification of the sequence of SEQ ID NO: 1 will effect the functional properties of SEQ ID NO: 1. The structure and function of one molecule does not provide guidance as to the structure and function of other molecules. Therefore, the description of one molecule (SEQ ID NO: 1) is not representative of a genus of homologues, splice, mutant and allelic variants of SEQ ID NO: 1 having unspecified functional activities different from that of SEQ ID NO: 1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of the

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claimed homologues, mutants, allelic and splice variants of SEQ ID NO: 1. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Response to arguments:

The response traverses the written description rejection. It is argued that the specification demonstrates that Applicant was in possession of the claimed genus of nucleic acid molecules. It is asserted that the specification describes gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic sequences, promoter sequences, and exogenous sequences.

These arguments have been fully considered but are not persuasive. A general statement in the specification of a desire to obtain gene sequences, homologues from other species, mutated species, SNPs, polymorphic sequences, promoter sequences and exogenous sequences is not equivalent to providing a clear and complete description of specific sequences which fall within the claimed genus of nucleic acids.

The response cites *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), in support of their argument that they have described the claimed genus of nucleic acids because they have disclosed the sequence of SEQ ID NO: 1.

However, the Court in *The Regents of the University of California v. Eli Lilly* held that "An adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan

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for obtaining the claimed chemical invention". While Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. In the present situation, Applicants have provided only a disclosure of a wish to obtain homologues, mutant, allelic, and splice variants of SEQ ID NO: 1. The specification does not disclose any specific mutant, allelic, or splice variants or homologues of SEQ ID NO: 1. Further, the functional activity of such variants is not disclosed. Accordingly, the specification has not disclosed a representative number of nucleic acid molecules within the claimed genus.

Applicants assert that they have disclosed the common structural features of the claimed nucleic acids, i.e., SEQ ID NO: 1. It is asserted that each of the claimed nucleic acids having 90-99% identity with SEQ ID NO: 1 share the same structural feature of the sequence of SEQ ID NO: 1.

However, the claims are not limited to nucleic acids which share this common structural feature. Rather, the claims encompass nucleic acids having 90-99.9% identity with SEQ ID NO: 1. Thereby, the claimed genus of nucleic acids do not share the same common structural feature of containing the sequence of SEQ ID NO: 1. Applicants have not disclosed what specific sequence information must be shared by the claimed genus of nucleic acid molecules in order to ascertain which nucleic acids share a common structural feature. The genus of molecules having 90-99.9% identity with SEQ ID NO: 1 includes individual species of nucleic acids which may vary from SEQ ID NO:

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1 at any given nucleotide position within SEQ ID NO: 1. When the individual species within the genus are compared to one another, together this genus comprises nucleic acids which vary at each and every nucleotide position within SEQ ID NO: 1.

Accordingly, the genus of nucleic acids are not considered to share a common structural feature – i.e., there is no specific structural property that is common to all members of the claimed genus if each of the individual nucleotides may be varied.

Further, the claims do not recite a functional requirement for any of the claimed nucleic acids and thereby encompass nucleic acids having distinct functional properties.

Applicants state that the specification has disclosed hybridization conditions and methods of mutagenesis and vectors and thereby one reading the present specification would understand that Applicants had possession sequences having 90-99% identity with SEQ ID NO: 1.

This argument has also been fully considered but is not persuasive because providing methods for making nucleic acid molecules is not equivalent to teaching specific nucleic acid molecules having specific biological functions. The specification does not disclose a single molecule within the genus of nucleic acids having 90-99.9% identity with SEQ ID NO: 1. The specification does not describe the location or identity of nucleotides which may be varied within SEQ ID NO: 1, and does not describe the functional activity or other biological role associated with such variants. The specification also does not disclose any specific variants of SEQ ID NO: 1 which have a functional activity or biological role distinct from that of SEQ ID NO: 1. Modification of a nucleic acid sequence by 1 to 10% can significantly alter the functional activity of the

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nucleic acid and the protein encoded thereby. The genus of nucleic acids claimed is large and variable, and potentially includes nucleic acids encoding for proteins having diverse biological functions. The specification discloses only one member of this genus, i.e., SEQ ID NO: 1. This is not sufficient to place one of skill in the art in possession of a representative number of molecules having the varied attributes and features of species within the claimed genus. Accordingly, it is maintained that the written description requirements have not been adequately met for the broadly claimed genus of homologues, splice, mutant and polymorphic variants of SEQ ID NO:1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

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Carla Myers
June 6, 2006


CARLA J. MYERS
PRIMARY EXAMINER